Living alone and activation of the renin-angiotensin-aldosterone-system: Differential effects depending on alexithymic personality features☆

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Objective: Living alone is considered as a chronic stress factor predicting different health conditions and particularly cardiovascular disease (CVD). Alexithymia is associated with increased psychological distress, less social skills and fewer close relationships, making alexithymic subjects particularly susceptible to chronic stress imposed by “living alone”. Only few studies investigated the renin-angiotensin-aldosterone-system (RAAS) activity in response to chronic stress. We aimed at evaluating the effects of “living alone” as a paradigm for chronic stress on RAAS activity and putatively differential effects depending on alexithymic personality features.

Methods: Alexithymia and serum concentrations of renin and aldosterone were measured in 944 subjects from the population-based SHIP-1 study. Subgroups were formed using the median of the Toronto Alexithymia Scale-20 (TAS-20) and a cohabitation status of “living alone” or “living together”. Analyses were adjusted for various psychosocial, behavioral, and metabolic risk factors.

Results: “Living alone” was associated with elevated plasma renin (p < 0.01, β = 0.138) but not aldosterone concentrations in the total sample. On subgroup level, we found associations of “living alone” and elevated renin concentrations only in subjects low in TAS-20 scores (p < 0.01, β = 0.219). Interactional effects of alexithymia × cohabitation status were found for the aldosterone-to-renin ratio (p = 0.02, β = −0.234).

Conclusions: The association of chronic stress imposed by “living alone” with increased RAAS activity contributes to explain the relationship of this psychosocial stress condition and increased risk for CVD. In contrast, alexithymic subjects may be less affected by the deleterious effects of “living alone”.

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1. Introduction

The number and quality of social relations have repeatedly been found as important predictors for different health conditions and particularly cardiovascular disease (CVD): In a recent meta-analytic review, Holt-Lunstad et al. investigated associations of actual and perceived social isolation on mortality. In their study, “living alone” in contrast to ‘living with others’ and social isolation, defined as pervasive lack of social contact, communication and social activities were used as objective measures while ‘loneliness’ reflected the subjective feeling of disconnectedness and not belonging. The authors found an average increased likelihood of mortality of 29% for social isolation, 26% for loneliness and 32% for living alone [1]. Regarding CVD, increased risks were found for subjects with reduced social network in general population samples as well as in clinical samples (for overview [2]). Case et al. found living alone as an independent predictor for the prognosis after myocardial infarction [3]. Other authors reported about suffering from objective social isolation [4] and lack of available [5] and perceived [6] social support as being associated with increased mortality in samples suffering from cardiac diseases.

Objective and perceived social isolation are considered as chronic stress factors going along with responses of different neuroendocrine systems which may, at least in part, account for the influence of poor social relationships on morbidity and mortality. There is consistent evidence for the hypothalamic-pituitary-adrenocortical (HPA-)axis and the sympathoadrenal-medullary (SAM-)system being activated in response to stress imposed by social isolation (for overview [7]).
activity of the renin-angiotensin-aldosterone system (RAAS) has been shown to be closely related to the HPA-axis and the SAM-system in stress response [8]. However, most existing studies concentrated on the effects of acute stress conditions on the RAAS, showing increased levels of plasma renin and angiotensin II after exposure to psychosocial stressors in rats [9] and humans [10]. Studies investigating the relationship of RAAS activity and chronic stress in general are mainly based on animal models showing in the majority an increase in plasma renin activity due to sympathetic activation [11], for overview [12]. In contrast, basal and acute stress-stimulated aldosterone levels were reduced in animals and humans exposed to chronic stress [12]. Häfner et al. investigated associations of renin and aldosterone levels with depression and “living alone” in a population based sample [13]. The authors found significantly elevated renin- and aldosterone-levels in subjects being depressed and living alone at the same time. However, the factors “depression” and “living alone” taken separately were not associated with an activation of the RAAS.

In the search for psychosocial factors influencing the risk for cardiovascular disease (CVD), personality styles have received considerable interest [2,14]: Alexithymia is a personality style characterized by the reduced ability to identify and communicate on one’s feelings, an impoverished fantasy life and a concrete, utilitarian thinking style [15]. Alexithymic subjects experience psychological distress as somatic symptoms which cannot be interpreted in a meaningful way [16]. The ability to identify and describe feelings has been shown to be crucial for emotion regulation, thus putting alexithymic patients at a higher risk for increased psychological distress [17]. Accordingly, alexithymia was found to be associated with various stress-related psychiatric and somatic health conditions, especially affective and anxiety disorders but also 5- to 60-year all-cause mortality after controlling for medical risk factors [18]. Mechanisms involved in the association of alexithymia and different health conditions have been shown to include subclinical inflammatory responses and particularly increased levels of C-reactive protein and pro-inflammatory cytokines [19–21]. Moreover, hypertension has repeatedly been shown to be associated with alexithymia [22–24].

Previous studies found associations of alexithymia with elevated resting state sympathetic tone, higher heart rate and blood pressure reactivity [25] and increased basal anticipatory cortisol levels prior to social stress exposure [26]. Hua et al. reported about associations of increased activity of the HPA-system with the “difficulties identifying feelings”-factor of alexithymia [27]. Tolmunen et al. described in their population-based follow-up study an increase in cardiovascular mortality being associated with alexithymia [28]. Investigating data from the same community-based sample as this study, Grabé et al. found associations of alexithymia, hypertension and subclinical atherosclerosis [29]. However, other researchers argued that alexithymia is rather related to increased symptom reporting than pathophysiologic changes: in their large population-based study on associations of coronary heart disease (CHD) and alexithymia, Kauhanen et al. found alexithymia being linked with previously diagnosed CHD, but not ischemia in an exercise tolerance test [30].

Alexithymic persons have been described as distant, less empathic and emotionally less attached to others [5,6]. Additionally, alexithymic patients are more often involved in social conflicts, as the differentiation of one’s own feelings from those of others is important for managing social relationships [31]. Lamy et al. found alexithymia being related to less perceived social support, fewer close relationships and less social skills [32]. In summary, alexithymic subjects having less social skills and reduced capacities to regulate psychological distress may be particularly susceptible to chronic stress imposed by the cohabitation status of “living alone”. This may result in activation of different neuroendocrine systems including the RAAS, thus representing a potential mechanism of how alexithymia and the risk for CVD are linked.

Results from previous studies suggest that depressive symptomatology may influence these relationships results in different ways: First, alexithymia has been shown to be strongly associated with depression [33,34]. Second, social isolation interacts with depression as living alone [35] and loneliness [36] increase the risk for developing depression, but also as common features of depression including social withdrawal and being hostile or irritable are likely to result in fewer social relationships and living alone. Finally, previous results suggested that individuals suffering from depressive symptoms show differences in stress reactions to “living alone” including altered RAAS activity [13]. Therefore, we included the lifetime diagnosis of major depressive disorder as a control variable in a second, fully adjusted model.

In detail, we tested the following hypotheses: (i) The cohabitation status of living alone is associated with elevated levels of renin and aldosterone. (ii) High TAS-20 scores are associated with elevated levels of renin and aldosterone, and (iii) ‘living alone’ and alexithymia interact such that subjects living alone and being highly alexithymic show increased levels of renin and aldosterone compared to the other subgroups.

2. Methods and materials

2.1. General population sample

We used data from the Study of Health in Pomerania (SHIP), a population-based cohort study conducted in the region of West Pomerania [37]. A multistage sampling scheme was adopted from the World Health Organisation’s MONICA Project, Germany. Adult German residents aged 20–79 years living in three cities and 29 communities in northeastern Germany were comprised in the sample. From the total population of 212,157, a sample of 7008 citizens was drawn from the resident’s registration offices in 1998. After exclusion of migrated or deceased persons, a net sample of 6265 eligible Caucasian subjects were comprised, out of which 4308 persons participated in the baseline stage (SHIP-0), corresponding to a response proportion of 68.8%. A first follow-up examination was conducted 5 years later and comprised 3300 subjects (SHIP-1). Alexithymia was assessed as part of an associated tele-ECG subproject. All 3300 subjects with available baseline and follow-up data were invited to take part in this project (Fig. 1). Mainly because of the complex nature of the project (ECG recording twice per day over a 1-month period at home) not > 1890 participated in the subproject. A total of 1874 TAS-20 questionnaires (99.15%) were returned; 430 were excluded due to missing values. All participants gave written informed consent to the study and scientific use of the data. The study conformed to the principles of the Declaration of Helsinki as reflected by an a priori approval of the Institutional Review Board of the University of Greifswald.

2.2. Analytic sample

Fig. 1 gives an overview of the selection process of our analytic sample. After exclusion of all participants with missing data in exposure, outcome or confounding variables, subjects with liver and renal disease (N = 27) were removed from the analytic sample. Additionally, pregnant women (n = 4) and participants with a regular intake of drugs acting on the RAAS including antihypertensive agents [anatomical therapeutic chemical (ATC) classification code C02], diuretics (ATC C03), beta-blockers (ATC C07), ACE-inhibitors (ATC C09A, C09B), angiotensin-receptor antagonists (ATC C09C, C09D) and calcium-channel blockers (ATC C08) (N = 421) were excluded, leaving a final sample of N = 944 female and male subjects.

2.3. Interview and examination

Sociodemographic factors including cohabitation status, past and current medication and behavioral risk factors were obtained by a computer-assisted face-to-face interview. All participants were asked to bring their packing containers of all medication they had been taking during the last 7 days as well as their drug prescription sheets.
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